

REMARKS

Previously, claims 44-63 were pending and under consideration. In the present paper, claim 44 has been amended. Thus, following entry of the present amendment, claims 44-63 will be pending and under consideration.

I. The Amendments to the Claims

In the present paper, claim 44 has been amended to recite, in relevant parts, “wherein the oligonucleotide is 100% complementary to SEQ ID NO: 3.” Support for the amendments may be found, for example, in the specification, at page 11, lines 8-11, and Example 15 at page 90, line 19 (Table 1, SEQ ID NO:27), as originally filed.

As the amendments to the claims are fully supported by the application as filed, they present no new matter. Accordingly, entry of the present amendments to the claims is hereby respectfully requested under 37 C.F.R. § 1.111.

II. The Rejection of Claims 44-52, 54-55, 58, 60, and 62 Under 35 U.S.C. § 102(e) Should Be Withdrawn

Claims 44-52, 54-55, 58, 60, and 62 stand rejected under 35 U.S.C § 102(e) as allegedly anticipated by Hancock *et al.* (U.S. Patent No. 6,534,277). The Patent Office alleges that Hancock *et al.* discloses an antisense oligonucleotide that is 27 nucleobases in length and comprises a 13 nucleobase consecutive stretch of instant SEQ ID NO: 27. *See* Office Action at page 3.

Without acquiescing to the propriety of the rejection and solely to expedite prosecution, Applicants have amended independent claim 44 to recite “An oligonucleotide 12 to 30 nucleobases in length, or a salt thereof, targeted to a nucleic acid molecule encoding apolipoprotein B, wherein the oligonucleotide is 100% complementary to SEQ ID NO: 3 and wherein the oligonucleotide comprises at least 8 consecutive nucleobases of SEQ ID NO:27.” Applicants respectfully submit that Hancock *et al.* does not teach an oligonucleotide that is 100% complementary to instant SEQ ID NO: 3. Instead, the oligonucleotide disclosed in Hancock *et al.* (SEQ ID NO: 32) is 55.6% complementary (15 out of 27 nucleobases) to instant SEQ ID NO:3.¹ As such, Hancock *et al.* fails to teach each and every element of independent claim 44 or dependent claims 45-52, 54-55, 58, 60, and 62 that incorporate the limitations of claim 44.

¹ SEQ ID NO:32 of Hancock *et al.*: 5'-CAC CTG GTT GTG TGC TAC CAT CCT ACT-3'
SEQ ID NO:3 of the present application: 3'-GAC ACA GTG AAC ACG ATG GTA GGG TAT-5'
(underline indicates base pair complementarity)

For at least the foregoing reason, Hancock *et al.* does not anticipate the presently pending claims. Accordingly, Applicants respectfully request that the rejection of claims 44-52, 54-55, 58, 60, and 62 under 35 U.S.C. § 102(e) over Hancock *et al.* be withdrawn.

III. The Rejection of Claims 44 and 48 Under 35 U.S.C. § 102(b) Should Be Withdrawn

Claims 44 and 48 stand rejected under 35 U.S.C § 102(b) as allegedly anticipated by Sanchez-Pescador *et al.* (U.S. Patent No. 5,618,674). The Patent Office alleges that Sanchez-Pescador *et al.* discloses an antisense oligonucleotide that is 30 nucleobases in length and comprises a 12 nucleobase contiguous portion of SEQ ID NO: 27. *See* Office Action at page 6.

As discussed above, Applicants have amended claim 44 to recite that the antisense oligonucleotide is 100% complementary to SEQ ID NO: 3. Applicants respectfully submit that Sanchez-Pescador *et al.* does not disclose an oligonucleotide that is 100% complementary to instant SEQ ID NO: 3. Instead, the oligonucleotide disclosed in Sanchez-Pescador *et al.* (SEQ ID NO: 62) is 50% complementary (15 out of 30 nucleobases) to instant SEQ ID NO:3.² As such, Sanchez-Pescador *et al.* fails to disclose each and every element of independent claim 44 or dependent claim 48 that incorporates the limitations of claim 44.

For at least the foregoing reason, Sanchez-Pescador *et al.* does not anticipate the presently pending claims. Accordingly, Applicants respectfully request that the rejection of claims 44 and 48 under 35 U.S.C. § 102(b) over Sanchez-Pescador *et al.* be withdrawn.

IV. The Rejection of Claims 44-63 Under 35 U.S.C. § 103(a) Should Be Withdrawn

Claims 44-63 stand rejected under 35 U.S.C § 103(a) as allegedly being obvious over Hancock *et al.* in view of Monia *et al.* (U.S. Patent No. 5,656,612), Bennett *et al.* (U.S. Patent No. 6,172,216), and Wengel *et al.* (U.S. Publication No. 2002/0068708A1). Applicants respectfully submit that none of the cited references, either alone or in combination, teach or suggest each and every element of the presently amended claims.

A. Legal Standard

The Supreme Court's decision in *KSR Int'l Co. v. Teleflex*, 127 S.Ct. 1727, (2007) provides guidance regarding exactly how the differences between the prior art and claimed invention are analyzed to assess the obviousness or non-obviousness of the claims. As the

² SEQ ID NO:32 of Sanchez-Pescador *et al.*: 5'-AAG ACC TAT AAC TTC TAC CAT CCC ATT TTG-3'
SEQ ID NO:3 of the present application: 3'-GAC ACA GTG AAC ACG ATG GTA GGG TAT GAA-5'
(underline indicates base pair complementarity)

Supreme Court explained, “interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art” can all be assessed “to determine whether there was an apparent reason to combine the known elements” as recited by the claim at issue. *See id.* at 1731. “[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *Id.* at 1741; *See also* M.P.E.P. § 2141 (8th Ed., Rev. 7, July 2008). Accordingly, the Patent Office must “identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in a way the claimed new invention does.” *Id.*

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *See In re Royka*, 490 F.2d 981 (C.C.P.A. 1974). “All words in a claim must be considered in judging the patentability of that claim against the prior art.” *In re Wilson*, 424 F.2d 1382, 1385 (C.C.P.A. 1970). In addition, one of ordinary skill in the art must have a reasonable expectation of success in achieving the claimed invention. *See In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

B. The Combination of References Does Not Teach or Suggest Each And Every Element of the Claims As Amended

The Patent Office alleges that the cited references teach an antisense oligonucleotide that allegedly meets the structural limitations of the claimed subject matter because Hancock *et al.* discloses an oligonucleotide that is 27 nucleobases in length and comprises a 13 nucleobase consecutive stretch of instant SEQ ID NO: 27. *See* Office Action at page 6. The Patent Office further alleges that it would have been obvious to modify the antisense compound of Hancock *et al.* to comprise the modifications disclosed in Monia *et al.*, Bennett *et al.*, and Wengel *et al.*

Applicants respectfully point out that claim 44 has been amended to recite that the antisense oligonucleotide is 100% complementary to SEQ ID NO: 3. Applicants respectfully submit that the combination of references cited by the Patent Office fails to teach or suggest an antisense oligonucleotide that is 100% complementary to SEQ ID NO: 3 of the present application. As discussed in detail above, SEQ ID NO: 32 of Hancock *et al.* is only 55.6% complementary to SEQ ID NO: 3 of the present application. Further, Monia *et al.*, Bennett *et al.*, and Wengel *et al.* do not cure this deficiency because the references fail to teach or suggest anything regarding antisense oligonucleotide sequences that are complementary to SEQ ID NO: 3 of the present application, much less teach or suggest antisense

oligonucleotide sequences that are 100% complementary to SEQ ID NO: 3. Instead, as acknowledged by the Patent Office, Monia *et al.*, Bennett *et al.*, and Wengel *et al.* disclose chemical modifications to antisense compounds or pharmaceutically acceptable carriers. *See* Office Action at pages 7-9. As such, the cited references fail to meet the structural limitations of the claimed subject matter.

Further, none of the references, whether considered alone or in combination, suggest modifying the disclosure of Hancock *et al.* or other cited references to select oligonucleotide sequences that are 100% complementary to SEQ ID NO: 3. In fact, the Patent Office acknowledges that "Hancock *et al.* does not teach wherein the disclosed oligonucleotide inhibits the expression of the long form of apolipoprotein B, ApoB-100." *See* Office Action at page 6. As such, the references fail to suggest a reason to target SEQ ID NO: 3 encoding apolipoprotein B, much less target specific portions of SEQ ID NO: 3 that are complementary to sequences comprising at least 8 consecutive nucleobases of SEQ ID NO:27. Without such suggestion, the Patent Office cannot establish obviousness under the controlling standard articulated by the Supreme Court. *See KSR*, 127 S.Ct. at 1741.

Thus, Applicants respectfully submit that none of the claims are obvious over the combination of references cited by the Patent Office. Accordingly, Applicants respectfully request that the rejection of claims 44-63 under 35 U.S.C. § 103(a) as obvious over Hancock *et al.*, Monia *et al.*, Bennett *et al.*, and Wengel *et al.* be withdrawn.

CONCLUSION

In light of the above remarks, Applicants respectfully request that the Patent Office reconsider this application with a view towards allowance. The Examiner is invited to call the undersigned attorney at (650) 739-3949, if a telephone call could help resolve any issues.

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Respectfully submitted,



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